

Extracting Putative Gene Coexpression Networks for Low Dose Ionizing Radiation using Combinatorial Algorithms

Gary L. Rogers¹, Sudhir Naswa¹, Rachel M. Lynch², Stephen A. Kania³, Suchita Das², Elissa J. Chesler^{2,4}, Arnold M. Saxton⁵, Brynn H. Voy^{2,5}, Michael A. Langston¹

¹Department of Electrical Engineering and Computer Science, University of Tennessee, Knoxville ;

²Systems Genetics Group, Oak Ridge National Laboratory, Oak Ridge, Tennessee; ³Department of Comparative Medicine, University of Tennessee, Knoxville; ⁴The Jackson Laboratory, Bar Harbor, Maine; ⁵Department of Animal Science, University of Tennessee, Knoxville.

Biological data generated through large scale -omics technologies have resulted in a new methodology in the study of biological systems. Instead of focusing research efforts on single genes or proteins, newer technologies enable us to extract entire biological networks using powerful computing and statistical algorithms that extend to extremely large datasets. We have developed a tool chain using novel graph algorithms to extract gene coexpression networks from microarray data. We demonstrate the use of our tool chain to investigate the effects of in vivo low dose ionizing radiation treatments on mice. We are using systems genetics approach to explore the biological effects of low dose (10 cGy) ionizing radiation. We measured the base line gene expression profile from spleen tissue of BXD recombinant inbred mice using Illumina microarrays. The data was filtered using coefficient of variance after applying robust spline normalization and variance stabilizing transformation. The data was transformed into a graph, with probes represented as vertices and edges between them representing correlation coefficients. The graph was analyzed using our tools to identify the size and number of maximal cliques. We deployed another tool, paraclique, which relaxes clique's strict requirement that every edge be present between all vertices. Paraclique allows us to account for inherent noise in the microarray data and stochastic nature of biological processes. Using immunophenotype data from the baseline BXD mice, we computed all correlation coefficients between all genotypes and immunophenotypes (%CD4, %CD3, LN T:B, %CD8, and LN CD4:CD8) and transformed the data into a graph. Bicliques between the two partitions were extracted and analyzed. We also extracted eQTLs from BXD data using QTL-Reaper from base line gene expression profiles. 1881 transcripts were associated with 686 loci. The eQTLs were classified as cis or trans according to their genomic positions. Besides population level studies we also investigated the differential effect of low dose and high dose (1Gy) of ionizing radiations on spleen gene expression in inbred parental strains (C57BL/6J and DBA/2J) of BXD recombinant inbred mice as well as BALB/c mice, a known radiation-sensitive strain.